7-23-91

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: Trifluralin: Reasons for not returning trifluralin to the peer review process for carcinogenicity

TO: Esther Rinde, Ph.D.
Manager, Peer Review Committee for Carcinogenicity
SACB/HED (H7509C)

FROM: Whang Phang, Ph.D. 7/23/91
Pharmacologist
Tox. Branch II / HED (H7509C)

THROUGH: James Rowe, Ph.D. 7/23/91
Section Head
and
Marcia van Gemert, Ph.D. 7/23/91
Branch Chief
Tox. Branch II / HED (H7509C)

Trifluralin has been scheduled for peer review in September, 1991. During the initial evaluation of the available toxicology data on this chemical, this reviewer has not discovered any new data which warrant returning this chemical to the HED peer review process for carcinogenicity.

In 1986, the Peer Review Committee had evaluated the toxicology data of this chemical and concluded that trifluralin produced an increase in the incidence of malignant or, combined malignant and benign tumors of the renal pelvis, and benign tumors of the urinary bladder. The chemical was classified as a Category C (possible human) carcinogen, and a Q_1* of 0.0077 was calculated.

In 1987, the registrant submitted a carcinogenicity study in NMRI mice. An increase in the incidence of hepatocellular carcinoma was seen in the high dose males (control, 1/50; high dose, 4/50). However, this increase was within the range of the historical control for hepatocellular carcinoma in male NMRI mice for the testing laboratory (Attachment A). No dose related response was found with respect to the liver tumor incidence. In November of 1989, the Deputy Director of HED, William Burnam called a meeting to discuss the findings of this study (Attachment B). "The consensus of the attendees was that incidence of male

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liver tumors found in the Hoechst trifluralin study was insufficient to cause trifluralin to be returned to the HED Peer Review Group".

This reviewer discussed these issues with Dr. Marcia van Gemert, Branch Chief, and she agreed that it would not be necessary to return this chemical to the peer review process for carcinogenicity.

trifluralin

Page_____ is not included in this copy.

Pages 3 through 6 are not included.

The material not included contains the following type of information:

____ Identity of product inert ingredients.

____ Identity of product impurities.

____ Description of the product manufacturing process.

____ Description of quality control procedures.

____ Identity of the source of product ingredients.

____ Sales or other commercial/financial information.

____ A draft product label.

____ The product confidential statement of formula.

____ Information about a pending registration action.

X FIFRA registration data.

____ The document is a duplicate of page(s) _____.

____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

11/29/89 ATTACHMENT B Shirley

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

AD HOC MEETING 11/21/89

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Trifluralin Mouse Cancer Study

FROM: William L. Burnam, Deputy Director
Health Effects Division (H7509C)

TO: Penelope Fenner-Crisp
Reto Engler
Karl Baetcke
Marcia Van Gemert
Hugh Pettigrew
Bruce Jaeger

The consensus of the attendees was that incidence of male liver tumors found in the Hoechst trifluralin study was insufficient to cause trifluralin to be returned to the HED Peer Review Group.

cc: Rick Tinsworth
Caswell File 889

Attachment

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Trifluralin Mouse Study

Issue: The initial review of Hoechst trifluralin mouse cancer study indicated a possible compound-related effect on liver tumors in males. Historical control data were requested. [redacted]

EPA - INTERNAL DELIBERATIVE INFORMATION.. NOT INCLUDED

Background: The attached peer review indicates that trifluralin was a C carcinogen based on positive effects in male and female rats. In males, it produced an increase in follicular cell adenomas and carcinomas in thyroid and malignant neoplasms of the renal pelvis; in females it caused an increased incidence of benign urinary bladder tumors. A Q_1^* of 7.7 X 10-3 is currently used for risk assessments based on the combined incidence of the above mentioned tumors. Trifluralin was not oncogenic in the B6C3F1 mouse at doses up to 4500 ppm.

Discussion: The male mouse liver data are as follows:

	Dose (ppm)			
	0	50	200	800
No. examined	50	50	50	50
Hepat. adenoma	5 (10)	8 (16)	7 (14)	6 (12)
Hepat. carcinoma	1 (2)	3 (6)	7 (14)	4 (8)
Combined	6 (12)	11 (22)	14 (28)	10 (20)

percents in (___)

According to Hugh Pettigrew, a pair-wise comparison of total liver tumors between the control and mid dose gives a value of P=0.039. The Peto trend analysis (attached) indicates that there is no significant trend for either the adenomas, carcinomas or combined adenomas and carcinomas.

The historical control information (attached) indicates that for similar studies of 2 year duration the average values for adenomas in males was about 10% (using the top 7 studies). The average value for carcinomas was about 3.4% for the same 7 studies. The controls in this study are very similar to past values while all treated groups are elevated. There is evidence from two of the studies that combined liver tumor values of 20% have occurred while another study showed a low of 4% combined incidence.